amounts of fat under conditions in which the normal fat depots give up almost their last molecule of fat.

SUMMARY. There is reported the microscopic and chemical examination of a retroperitoneal liposarcoma without myxomatous elements, weighing sixty-nine pounds, being the largest solid tumor of which we can find record. It illustrates the capacity of malignant tumors to store up protein and fat, despite extreme emaciation of the host.

VASCULAR REACTIONS IN VASCULAR HYPERTENSION.[1]

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A STARTLING observation, made two years ago, was directly responsible for the following study:

The patient was a woman, aged forty-eight years, with an extremely high blood-pressure and a normal renal function, one of those cases familiarly known as "vascular hypertension." Her systolic pressure had just been found to be 270, when the patient complained of rather severe cardiac pain. Nitroglycerin, gr. $\frac{1}{100}$, was given for relief. Curiosity led me to watch its effect on the blood-pressure. I was very much disturbed to find the pressure falling rapidly until it reached 110. In the meantime the patient had become very uncomfortable and was almost in collapse. An intravenous injection of adrenalin restored the pressure as quickly as it had fallen, and the patient become more comfortable.

This observation was so amazing that I was stimulated to study the reaction to nitroglycerin of the bloodvessels in this type of case. (I should state, at this point, that the above observation was unique on my part, none of its kind having since been made.) In the course of the investigation on the effect of nitroglycerin it was noted that during the preliminary period of our experiments, while we were trying to establish a base line before giving the drug, there was often a marked fall in pressure, due to rest and quiet. If exciting noises occurred near the patient, however, the pressure often rose to a surprising degree. The variations in pressure were so marked that we were led to determine not only the effect of nitroglycerin but also that of rest, excitement, exercise and afterward adrenalin. These results were interesting and instructive enough to warrant this report.

While some of the earlier experiments were, for obvious reasons,

[1] Study made under a grant from the Proctor Fund of Harvard University.

not done under standard conditions, the majority of those reported were carried out in the following manner: The patient was placed in bed in a quiet room for twenty to forty-five minutes. The object of this was to put him at his ease. At the end of this preliminary period the systolic and diastolic pressures and the pulse-rate were noted at five-minute intervals. Usually these patients established their base lines in thirty to forty-five minutes. Then I endeavored to excite the patient by urging him to talk about some disturbing subject. Generally his "high blood-pressure" (on which most of these patients are terribly centered) or his irritability, or some similar subject, was a sufficient excitation. It would, perhaps, have been somewhat better to have some standard form of excitation, such as that used by Meakins and Wilson in their study on "Irritable Heart,"[2] but no such means seemed practical or necessary. During the short two- or three-minute period of excitation, readings were again made and then the patient was allowed to become quiet again. After a sufficient time had elapsed to re-establish the base lines the effect of exercise—usually lifting from a reclining position to a sitting one ten times—or the effect of nitroglycerin under the tongue was tried. The adrenalin test was carried out in a similar way on another day. The doses of the drugs are given in the tables. Each observation consumed from one and a half to three or more hours on two days.

The first reaction to consider—the effect of quiet and rest—can be followed in Table I.

Here it can be seen that in the large proportion of the cases there was a definite and marked fall in both systolic and diastolic pressures during the preëxcitation period. In a very few, however, there was essentially no fall. In the systolic pressure the variations in the curves ranged from 0 to 46 mm., with an average of 21 mm. In the diastolic the fall varied from 0 to 18 mm., with an average of 10 mm. The time necessary to establish such falls varied markedly, as did the degree of fall, both being largely dependent on the nervous tension of the patient. The limits were from five to seventy minutes.

I presume that the following sequence of events took place in these patients. In spite of the preliminary rest period many were very nervous when the blood-pressure was first determined. As a result the pressure rose above its previous undetermined level. As the patient became accustomed to this maneuver the pressure fell. That this was true is indicated by the fact that the second and third readings were occasionally higher than the first. These were followed by the usual fall.

The effect of excitement showed a greater change in the pressure curves in the opposite direction. In every case there was a sharp rise. This was generally greater than the corresponding fall in the

[2] Heart, 1918, No. 1, vii, 17. In this study a pistol shot was used as a means of excitation.

preliminary period. The variations in the systolic pressures ranged from 10 to 52 mm., with an average of 30 mm. The diastolic pressures showed similar but less marked rises varying from 8 to 24 mm., with an average of 12 mm. In general, the rise was a very sharp one, the height of pressure being reached at the first determination. In some there was a rise at this reading, but the curve continued to ascend, reaching its maximum in ten to fifteen minutes.

TABLE I.—EFFECT OF REST AND EXCITEMENT IN VASCULAR HYPERTENSION.

Med. No.	Blood-pressure at start.		Maximum fall in mm. due to rest.			Maximum rise in mm. due to excitement.			Stimulus.
	Syst.	Diast.	Syst.	Diast.	Time in min.	Syst.	Diast.	Time in min.	
8022	126	98	3	18	40	10	8	5	Talking about a quack.
53819	148	92	30	16	65	24	8	15	Talking about father's death, etc.
7761	150	84	10	4	70	24	10	10	Talking about self and school work.
11704	152	98	14	2	20	34	24	15	Talking about blood-pressure and operation.
10664	172	98	18	2	20	40	10	5	Talking about her family.
6596	186	98	−1	5	30	20	8	5	Talking about her invalid daughter.
8976	186	110	0	0	—	52	10	5	Talking about her irritability.
8020	192	98	12	0	5	28	9	10	Thinking of a dead pet cat.
9799	198	99	23	10	40	—	—	—	Rest only.
9799	202	80	46	18	50	28	16	5	Talking about her school.
7608	209	92	35	10	60	50	10	5	Talking about her divorce.
8742	214	128	14	8	25	19	10	5	Talking about blood-pressure.
9846	222	122	—	—	—	36	8	10	Talking about self.
9846	227	122	10	12	20	32	24	15	Talking about blood-pressure.
6877	230	108	27	14	30	28	12	5	Talking about an attack of angina.
11581	238	104	26	1	65	16	9	10	Talking about blood-pressure.
Extremes	..	..	0-46	0-18	5-70	10-52	8-24	5-15	
Average	..	..	21	10	..	30	12		
					Controls.				
Manuel	114	64	4	4	10	14	10	5	Talking about exam.
F. Smith	116	62	6	2	20	14	6	5	Talking about exam.

In this and subsequent tables some of the cases do not seem to be hypertensive. They are, however, patients who have been many times hypertensive. By "time in min." is meant the time elapsed in reaching the maximum rise. The averages at the bottom of the table are only of those showing a positive rise. Two normal cases are included at the bottom of the table for comparison.

The effect of exercise in these hypertensive cases (Table II) showed somewhat conflicting results, as in normal cases. In general there was a fairly definite rise in both systolic and diastolic pressures. In one there was no rise in either. In two more there was a fall in the systolic and in five there was a fall in the diastolic pressure. The usual type of curve was a sharp rise followed by a fall almost as sharp. Rarely this is reversed. The results are similar to what occurs in normal individuals. The psychic element undoubtedly

plays a part in the reaction. The results are of special interest, however, in that they show how marked and how sudden a change may take place in these hypertensive patients as a result of moderate effort. A rise of 57 mm. in a normal patient is of much less significance than in a patient who already has a high pressure. (See Case No. 6596.)

TABLE II.—EFFECT OF EXERCISE.

Med. No.	Blood-pressure before exercise.		Maximum rise from exercise.		
	Systolic.	Diastolic.	Systolic.	Diastolic.	
53819	120	70	0	0	
8533	128	—	−4	—	
10664	132	84	10	−6	
7761	140	92	20	−2	
11704	142	100	16	0	
9709	162	80	26	8	
7608	168	82	45	0	Somewhat tired.
9709	170	80	42	4	
6596	184	98	57	22	
8976	186	120	10	−4	Tired.
10032	194	112	32	18	
8742	202	118	8	4	
6877	218	104	30	18	Tired.
8846	222	122	−20	−10	On repetition later; no fall in pressure from exercise.
Extremes	..	..	−20-70	−10-22	

It is of interest to note that while the diastolic pressures in the above experiments were more stable than the systolic they were far from being fixed. A variation of 24 mm. in the diastolic pressure within a two-hour period is indeed surprising. (See Case No. 8846, Table I.)

The observations recorded above may be merely exaggerations of what occurs normally. But in the hypertensive case they are of vastly greater significance. Furthermore the recognition of the fact that such wide variations in pressure can occur within a comparatively short period due to such commonplace causes as those used, is of extreme importance in estimating the meaning of any given high pressure. It must, too, make us very cautious about the interpretation of the effects of treatment. If a patient's pressure under the influence of mental and physical rest can drop 35 mm., and then under the excitation of talking about family difficulties can rise again 50 mm. (see Case No. 7608, Table I; see also same case, Table II) one can readily understand the wide variations that must take place every day in this type of case. One can understand, too, of how little significance are even moderate changes noted from time to time unless they are all in the same direction.

As a result of such observations as these I have become very skeptical about the therapeutic value of drugs, electricity, baths, etc., in this type of case. If they produce any effect at all it is largely through the accompanying mental or physical rest imposed.

Unless one can show a permanent or at least a long-continued lowering of pressure of a considerable degree, one cannot rightfully claim that any given therapeutic maneuver has been beneficial. I have yet to see a fall in pressure resulting from any method of treatment (except rest) that cannot be duplicated or exceeded by those observations we have made on rest. By the latter means one may reduce the pressure markedly, but, unfortunately, on the resumption of effort it rises again. However, with care it need not rise to its former level. After all, this is as much as we should reasonably expect, except in the earliest cases.

Another thought arises out of this study. The extreme liability of the vasomotor system in this type of case, as indicated by the marked and sudden changes in pressure, makes us wonder what the effect on the vessels must be. Will not these patients show earlier and more marked sclerosis of the vessel walls?

TABLE III.—EFFECT OF NITROGLYCERIN.

Med. No.	Blood-pressure at start.		Primary rise in mm.		Primary fall in mm.		Time in min.	Secondary fall in mm.		Time in min.	Dose in G.	
	Systolic.	Diastolic.	Systolic.	Diastolic.	Systolic.	Diastolic.		Systolic.	Diastolic.			
53819	148	92	4	0	—	—	—	2	16	15	0.0006	Slight reaction.
11704	152	98	22	22	—	—	—	2	0	30	0.0009	
10664	154	100	20	2	—	—	—	22	18	35	0.0009	
6596	186	98	20	4	—	—	—	5	6	35	0.0009	
8976	186	110	14	16	—	—	—	18	8	30	0.0009	
9799	188	90	24	11	—	—	—	19	14	50	0.0009	
9767	190	112	10	10	—	—	—	3	2	15	0.0006	
7608	209	92	26	10	—	—	—	22	8	45	0.0009	
6877	230	108	11	21	—	—	—	6	0	20	0.0009	
9106	238	154	5	16	—	—	—	25	0	20	0.0009	
10962	288	172	10	—	—	20	15	20	—	10	0.0009	
7761	128	92	—	—	16	42	23	—	—	—	0.0009	Some doubt about diast. pressures.
9767	190	112	—	—	2	2	5	−8	−10	15	0.0006	See above 9767.
8920	106	120	—	14	28	—	14	60	31	244	0.0006	
8880	212	102	—	14	32	—	23	—	4	—	0.0006	
11581	238	104	—	12	22	—	7	—	—	—	0.0009	

This table is divided into two parts. The first 11 cases are those which showed a primary rise. The others showed a primary fall. The last three in the second group showed no primary rise in the systolic pressure but a rise in the diastolic. One case in the first group showed a rise in systolic pressure and a fall in the diastolic.

In studying the effect of nitroglycerin in this disease we received two genuine surprises (Table III). Instead of finding a sharp fall of pressure after a fairly large dose of this drug placed under the tongue we found that the majority of our cases showed a primary rise. This, too, occurred during the height of the symptomatic reactions to the drug. The patient was flushed. There was pounding in the head and in the region of the heart. The radial pulses were definitely more full, and yet the systolic and diastolic pressures

were higher at this period instead of lower. Furthermore, these rises were not always trifling, being over 20 mm. in several cases. I am of the opinion that in these strikingly nervous people the excitement produced by the nitroglycerin caused the primary rise.

The second surprise was in the comparatively slight depressor effect of the drug. The drop in pressure, either following the primary rise or when there was no such rise, was comparatively slight. I say this in spite of the apparent contradiction in Table III. If one notices those cases in which a considerable fall took place after the nitroglycerin, he will see that, for the most part, it required a very long time to reach this depth. I cannot help feeling that much of this fall must be attributed to rest and quiet, otherwise, it seems to me, we should obtain the greatest drop during the period of vasodilatation, *i. e.*, during the period of flushing, increased pulse volume, etc.

Observations like these confirm our ideas about the uselessness of nitroglycerin in hypertension. Formerly we discarded this drug on the grounds that the depressor effect was too transient to be of value. These experiments of ours show that there is but little reduction of pressure due to the drug and that there is often a primary rise in pressure. Rest alone is far more effective.

TABLE IV.—EFFECT OF ADRENALIN.

Med. No.	Blood-pressure at start.		Maximum rise in mm.		Time in min.	Duration of rise.	Dose in c.c.	Remarks.
	Syst.	Diast.	Syst.	Diast.				
7761	132	90	42	50	2	20	0.5	
8533	134	48	48	10	10	45	0.5	Plateau curve.
53819	140	80	30	12	2	60	0.5	Rather prolonged rise.
11704	160	104	80	−40	2	25	0.5	Sharp, marked rise.
10664	166	98	52	10	2	22	0.5	Double rise.
7608	194	90	40	10	24	120	0.5	Slow rise and fall; typical syndrome reaction.
6877	199	94	70	22	5	40	0.5	Double rise; angina.
8076	200	120	26	10	10	15	0.25	Too small a dose.
6506	206	104	87	22	2	95	0.5	Sharp rise and fall, the latter trailing off; angina.
8846	214	118	8	−2	2	6	0.5	? about site of injection.
Extremes	..	..	26-87	10-50	..	15-120		
Average	..	..	53	18				
					Controls.			
Munnel	114	62	8	2	4	55	0.5	Normal student.
De Blois	100	60	14	10	2	50	0.5	Gastric necrosis.

Only 2 normal cases are included at the bottom of the table for purposes of comparison. For normal controls, see report of work at Lakewood.

In spite of the above, nitroglycerin has a place in the treatment of one of the complications of vascular hypertension. Clinical experience has taught us its value in angina pectoris. In the light of our results one cannot help wondering about the effect of this drug on the various bloodvessels of the body. There is no doubt that it

causes a vasodilatation of many of the vessels. This can be seen and felt. No doubt, too, in angina the relief comes from such a vasodilatation, and yet there is a compensating or overcompensating mechanism in this disease which maintains the pressure at a high level in spite of the nitroglycerin.

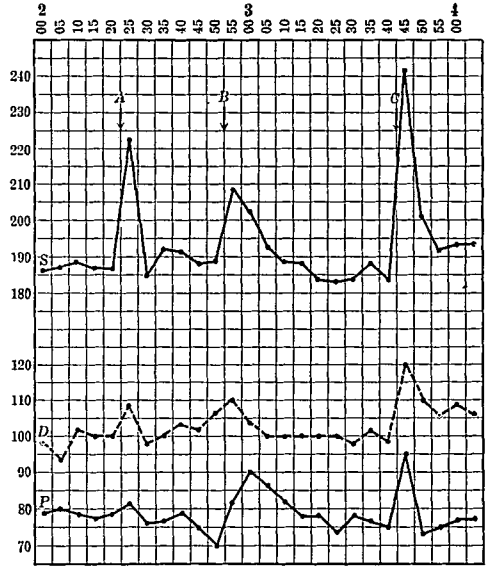

CHART I.—In this chart and those that follow, the ordinate indicates time, the abscissa, pressures, pulse and respiration rates. *S*, systolic blood-pressure; *D*, diastolic blood-pressure; *P*, pulse-rate; *R*, respiration-rate. In the diastolic pressure curve the symbol O is occasionally used. This indicates that no abrupt change from a sharp to a muffled note was heard but merely a gradual decrease in sounds. The O represents the level at which the last sound was heard. Chart I demonstrates the effect of emotion, nitroglycerin and exercise. At *A* is noted the effect of talking two minutes about an invalid daughter. At *B* nitroglycerin, 0.0009 G., was given under the tongue. Note especially the rise of 20 mm. in the systolic pressure and the comparatively negligible fall of this pressure. At *C* the patient lifted herself from the reclining to the sitting position ten times.

One of the most interesting phases of this study of ours is that of the effect of adrenalin, as in the Goetsch test.[3] Sturgis and Wearn,[4] at Lakewood, have shown that ½ c.c. of a 1 to 1000 solution of drug given intramuscularly in normal individuals causes no appreciable rise in blood-pressure.

[3] New York State, Jour. Med., July, 1918, xix, 259.
[4] Arch. Int. Med. September, 1919, xxiv, 269.

Our data is very meager consisting of only ten cases. This small number is due to the fact that we became afraid to use the drug in this type of case. The reaction was so striking and so nearly constant that we feel it worth while to report our cases. In only one case (No. 8846, Table IV) did we fail to get the typical reaction. In this one case there was some doubt about the technic.

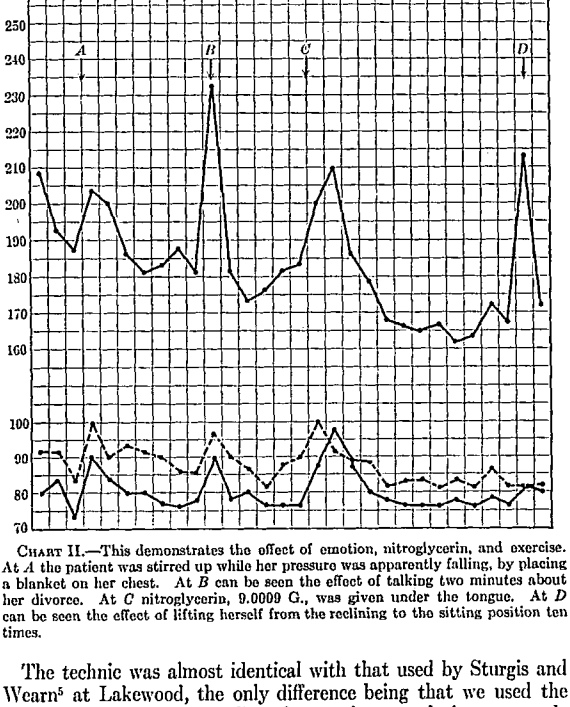

CHART II.—This demonstrates the effect of emotion, nitroglycerin, and exercise. At *A* the patient was stirred up while her pressure was apparently falling, by placing a blanket on her chest. At *B* can be seen the effect of talking two minutes about her divorce. At *C* nitroglycerin, 9.0009 G., was given under the tongue. At *D* can be seen the effect of lifting herself from the reclining to the sitting position ten times.

The technic was almost identical with that used by Sturgis and Wearn[5] at Lakewood, the only difference being that we used the prepared solution of adrenalin, whereas there a solution was made from tablets. The patient was kept at rest in bed in a quiet room for one-half to one hour. Control pressure readings, pulse and respiration rates, symptoms, etc., were then noted at five-minute intervals until a base line was established. Then ½ c.c. of a 1 to 1000

[5] Sturgis and Wearn, cited above.

solution of adrenalin was injected into the deltoid or biceps muscle. Pressure readings, etc., were thereafter made every two minutes for ten minutes, then every five minutes for one hour or more, and then every ten minutes until the pressure came back to normal.

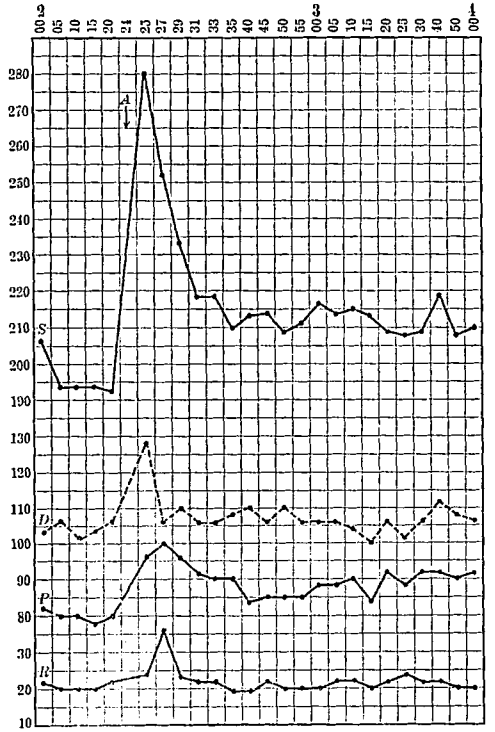

CHART III.—This demonstrates the effect of adrenalin. At *A* the patient was given 0.5 c.c. adrenalin (1 to 1000) intramuscularly. Note the sharp, terrific rise in pressure.

The reaction to the drug was striking and in some instances alarming. A typical one showed a sharp rise of pressure averaging 53 mm. for the systolic and 18 mm. for the diastolic. In two cases the maximum systolic rise was over 80 mm. When such a rise took place within two minutes after the drug was injected it was indeed striking, especially if it started from a base line of over 200 mm.

Generally the pressure was not maintained at the high level for longer than a few minutes. It then fell, sometimes fairly abruptly and sometimes more gradually. Occasionally there was a secondary slight rise during the fall. The time required to reach the maximum pressure and to reach the former level is indicated in Table IV. Immediately after the injection of the drug the patient became pale

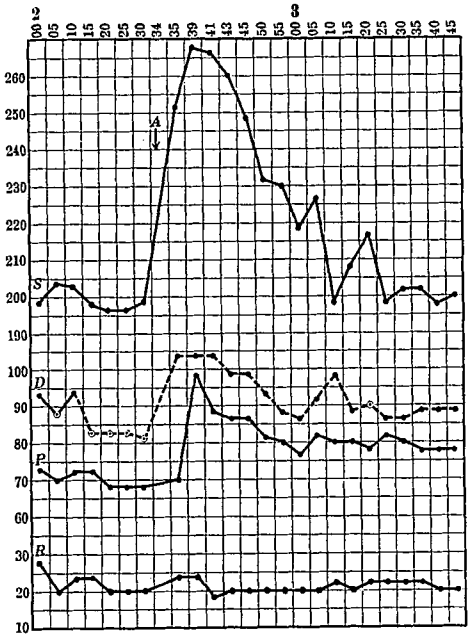

CHART IV.—Another adrenalin effect. At *A* the patient was given 0.5 c.c. adrenalin (1 to 1000) intramuscularly. Patient had severe angina pectoris.

and tense and had a feeling of tingling all over. There was sometimes a slight tremor of the hands and usually a pounding in the head and in the region of the precordia. In one or two there were practically no symptoms.

Neither in the symptomatology nor in the pressure curves did our cases resemble those of the "effort syndrome" reported from Lakewood. Only one case (No. 7608, Table IV) showed the typical "syndrome curve," but this patient did not display the symptoms which are so characteristic.

A few of the curves resemble more closely those reported by Goetsch in his hyperthyroid series, especially those with the secondary rise (Nos. 10664 and 6877, Table IV). As a rule, however, our cases showed a much more abrupt and higher rise than did those of Goetsch. That these patients were cases of hyperthyroidism is not at all credible. In fact, we have determined the basal metabolism on a few that seemed possibly thyrotoxic and found it to be subnormal instead of raised.

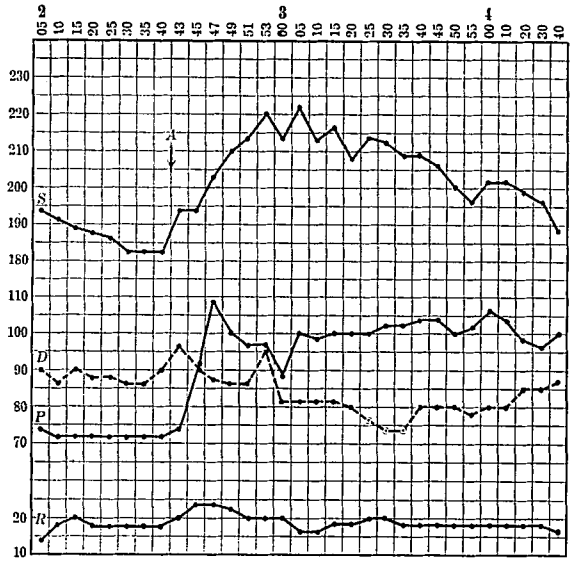

CHART V.—Another adrenalin effect. At *A* patient was given 0.5 c.c. adrenalin (1 to 1000) intramuscularly. Note the more slow and sustained rise in pressure. This resembles the reaction obtained by Goetsch in his hyperthyroid cases.

Two cases in this series warrant special comment because of the alarming nature of the reaction. Case No. 6877 was an elderly woman who had had several attacks of rather mild angina pectoris. After the injection of adrenalin the pressure rose immediately 70 mm. The patient became very pale and frightened and had the worst attack of angina she had ever experienced. Fortunately the pressure fell rather promptly and the symptoms abated as quickly.

The second case (No. 6596) showed a similar alarming jump in the systolic pressure from 193 to 280 in one minute. She, too, became very pale and frightened and had a tremendous sense of constriction in the region of her heart.

Both of these patients felt they were going to die and I was much alarmed. It was a great relief to see the pressure fall instead of continuing to rise.

Cases like these made me unwilling to try this reaction further in patients with a pressure over 190 mm. Consequently my series is small. They should serve as a warning against indiscriminate use of adrenalin intramuscularly.

The "adrenalin reactions" in hyperthyroidism, the effort syndrome and in vascular hypertension are interesting problems requiring much more study. In the last group the worker must realize that he is "playing with dynamite."

It is safe to conclude from these studies that:

1. The vasomotor system in vascular hypertension is extremely labile and sensitive.
2. Mental and physical rest causes a marked fall in pressure.
3. Excitation causes a more marked abrupt rise.
4. Exercise usually causes a similar rise.
5. Nitroglycerin produces practically no fall in pressure and there is often a primary rise following its absorption.
6. The vessels are especially sensitive to the intramuscular injection of adrenalin, a marked rise in pressure taking place immediately after its injection.

I gratefully acknowledge the assistance of Miss Elsa Griffin.

THE DANGERS OF ASCARIASIS.

By Bowman Corning Crowell, M.D.,
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Animal parasites of the human host are today probably attracting more attention than ever before, while with improved modern methods new ones are being discovered, and, as the result of accumulated knowledge, pathogenic properties are being ascribed to those formerly considered harmless. The technic of the laboratory is being employed in all its refinements to aid in diagnosis, and, on the other hand, treatment of some forms of intestinal parasitism is being carried out on a more scientific basis and on a larger scale than could have been foreseen only a few years since. International campaigns against parasites are now taken in a matter-of-fact way, and the mention of their scope in all their vast inclusiveness excites little more than passing admiration.